Chapter Two

Molecular Recognition in Crystalline Nitro Compounds Using C-H...O Hydrogen Bonds
2.1 Introduction

The emergence of supramolecular chemistry as a major area of research has been accompanied by the corresponding study of the intermolecular forces which must be implicated in the self-assembly of molecular components into supramolecular species with pre-desired architectural and functional features. Most of these efforts have concentrated on strong or conventionally hydrogen bonded O-H...O or N-H...O building blocks (carboxylic acid, pyrimidine, aminopyridine, acylaminopyridine) and are necessarily limited to a small number of substances. Yet, the scope of supramolecular assembly can be enhanced considerably if one considers, in addition, weak intermolecular interactions. The C-H...O hydrogen bond is one such weak interaction with potential for solid state supramolecular assembly. C-H...O based supramolecular design is interesting because most organic compounds do not contain functional groups capable of strong hydrogen bonding and in such instances one ought to be able to consider C-H...O interactions for the design of new supramolecular structures. Additionally, consideration of these interactions is useful even in strongly hydrogen bonded materials because it can reveal secondary and tertiary structural features which are often crucial to the optimisation of specific properties of these materials. The co-existence of these weak and strong hydrogen bonds may at times offer suitable explanations for anomalies in the patterns of strong hydrogen bonds (see Chapter 3) and rationalise the structural features of biological molecules.

Though the energy of C-H...O hydrogen bonds is only in the range of 1-5 Kcal/mol, the interaction is directional. In addition, for successful molecular recognition the selective and directional binding of the substrate by a molecular receptor is important and not the strength by which the receptor interacts with the substrate. Of course, the strength of the interactions becomes important when there is competition. So, the weak C-H...O hydrogen
bonds can effectively be used in molecular recognition and the present work is aimed to demonstrate this fact.

\[ \text{Scheme I} \]

The idea of employing C-H...O hydrogen bonds in molecular recognition traces back to the statement of Dannenberg that, the '...H bonding between the nitro and amino groups is precluded by the methylation of the amino groups.' (Scheme I)\(^9,10\) So this project was initiated basically to look at the C-H...O hydrogen bonds of NMe\(_2\) with NO\(_2\), 1-3, because it is well known that the CH\(_3\) group is a good C-H...O bond donor.\(^11\) Further, a few other molecular complexes of nitrobenzoic and nitrocinnamic acids, 4-11 prepared for various other reasons also revealed a systematic trend in C-H...O hydrogen bonding. These results warranted a detailed study of C-H...O recognition patterns in nitro compounds. The C-H...O patterns are discussed based on exhaustive searches of the Cambridge Structural Database (CSD)\(^12\) and an attempt is made to formulate some guidelines for the effective practice of nitro group crystal engineering with C-H...O interactions.

Cooperativity is a distinctive property associated with supramolecular
assembly and this phenomenon has been well-studied for strong hydrogen bonds both experimentally\textsuperscript{13} and computationally.\textsuperscript{14} There is no corresponding study for C-H...O hydrogen bonds, though it is assumed that this property is operational in these bonds.\textsuperscript{46} Cooperativity permits additional stabilisation to supermolecules to overcome entropic barriers.\textsuperscript{14} A dimer must be stabler than a monomer, a tetramer stabler than a pair of dimers and so on; otherwise the molecular (or oligomeric) species would be preferred to the supramolecular species. The energy of cooperativity is a crucial resource for self-assembly via weak intermolecular interactions. For the first time the cooperativity in C-H...O hydrogen bonds is visualised in this study.

\begin{align*}
1a. & \quad R_1 = R_3 = H; R_2 = NO_2 \\
1b. & \quad R_1 = R_3 = NO_2; R_2 = H \\
1c. & \quad R_1 = R_3 = H; R_2 = N(CH_3)_2 \\
1d. & \quad R_1 = R_3 = H; R_2 = NH_2 \\
2a. & \quad R_1 = R_3 = R_4 = H; R_2 = NO_2 \\
2b. & \quad R_1 = R_3 = NO_2; R_2 = R_4 = H \\
2c. & \quad R_1 = R_3 = H; R_2 = R_4 = NO_2 \\
2d. & \quad R_1 = R_3 = R_4 = H; R_2 = N(CH_3)_2 \\
2e. & \quad R_1 = R_4 = OCH_3; R_2 = R_3 = H \\
2f. & \quad R_1 = R_2 = OCH_3; R_3 = R_4 = H
\end{align*}
The numbering scheme used for the compounds la-ld, 2a-2f and complexes, 1-10 will be maintained in the subsequent chapters also.

### 2.2 Results and Discussion

#### 2.2.1 C-H...O Hydrogen Bond Patterns in Complexes 1 and 2 and Cooperativity

In complex 1 (Figure 1), a linear ribbon that comprises O-H...O and C-H...O dimers (X) is the main structural element. The two acid molecules are linked by O-H...O hydrogen bonds of 2.606(3) and 2.632(3)\(\AA\) to form dimers and both the carboxy groups are completely disordered (C-O, 1a, 1.26 and 1.26\(\AA\)and 1c, 1.28 and 1.27\(\AA\)). More interestingly, these dimers are themselves organised using two C-H...O bonds involving NO\(_2\) and N(CH\(_3\))\(_2\) groups to form dimer X (C...O 3.658(4), 3.725(4)\(\AA\); H...O 2.71(3), 2.71(3)\(\AA\); C-H...O 164(2), 172(2)°). It is worth noting that the H atoms of the CH\(_3\) groups were located from difference-Fourier syntheses and are ordered. The low R-factor and positional e.s.d.s allow one to make confident statements regarding the position of the H atoms. The conformations of the two CH\(_3\) groups are such that the two C-H...O angles within the C-H...O dimer are very close to 180°. The relevant H atoms lie only 0.11(3) and 0.16(3)\(\AA\).
Figure 1. O-H...O and C-H...O Hydrogen bonds in the crystal structure of complex 1. Notice the dimer rings formed in each case. N = ● O = ⊙
from the mean C-H...O dimer ring plane (atoms NO$_2$, NC$_2$) and the angle between the NO$_2$ and NC$_2$ planes is only 8.4°. It is to be mentioned here that the ordering of the CH$_3$ group and its directional specificity has been unequivocally demonstrated by Dunitz and coworkers in a tri-hydrated tricyclic orthoamide, where an energy of 1.8 Kcal/mole was estimated for each of the three C-H...O hydrogen bonds formed by the CH$_3$ groups with water O atoms.$^{11}$

Complex 2 also forms a similar linear acentric molecular ribbon which is characterised by a carboxyl O-H...O heterodimer (O...O, 2.570(3), 2.657(3)Å) and the C-H...O dimer X (Figure 2). The carboxyl group of acid 1a is fully disordered (C-O, 1.26, 1.27 Å) while that of acid 2d is partially disordered (C-O 1.25, 1.28Å). Figure 2 shows that dimer X obtained in complex 2 has bifurcated (3-centred) C-H...O interactions$^{15}$ instead of two linear C-H...O hydrogen bonds as obtained in complex 1. A H atom of the N(CH$_3$)$_2$ group is bifurcated by the two NO$_2$ O atoms while one of the NO$_2$ O atoms forms C-H...O bonds with two H atoms. Hence dimer X in complex 2 is more properly represented by three C-H...O interactions, C...O, 3.618(5), 3.700(5), 3.803(5)Å, H...O 2.82(4), 2.80(4), 2.88(4)Å and with the C-H...O angles being 147(3)°, 168(3)°, 164(3)°. The H atoms of the CH$_3$ groups were located from difference Fourier maps and are ordered, with the six C-H bond lengths being in the range 0.91-1.06(4)Å. Notably the two H atoms of dimer X lie within the plane of the C-H...O dimer (0.08(5) and 0.10(5)Å). Also the NO$_2$ and NC$_2$ planes of this complex make an interplanar angle of 8.76°, so the whole arrangement is quite planar.

It was also attempted to prepare single crystals of complex 3 (2a : 2d) to observe the binding characteristics between these two electronically differently substituted cinnamic acids but the poor quality of the crystals did not permit any X-Ray studies. Yet another attempt was to build a linear chain exclusively with dimer X (for example, see Figure 3) and for this pur-
Figure 2. O-H...O and C-H...O Hydrogen bonds in the crystal structure of complex 2. The 1a and 2d molecules form a linear chain. Notice that dimer X is comprised of bifurcated C-H...O bonds unlike in complex 3. N = ● O = ○
pose, a complex 11 of 1,4-dinitrobenzene and N,N,N',N'-tetramethyl- p-phenylenediamine was prepared but the diffraction data on this twinned crystal were so poor that though an approximate structure was obtained, it failed refine. This rough structure with an R-value of 0.15 hints at the possibility of a NO$_2$-N(CH$_3$)$_2$ recognition pattern, but it appears that the C-H...O hydrogen bonded chain is criss-crossed instead of being linear and probably involves bifurcated C-H...O interactions.$^1$

The change of the donor species from 1c to 2d in complexes 1 and 2 does not alter the gross recognition features of the NO$_2$ and N(CH$_3$)$_2$ groups but the relative approach of groups is altered slightly. This example indicates that the exact nature of dimer X is dependent on the molecular geometry and other (isotropic) crystal packing forces present in the solid. Such substitutional changes (like 1c $\rightarrow$ 2d) are of interest and significance because the conjugation (hyperpolarisability) in the chain increases and this property is of relevance in the design of NLO materials.$^{16}$

It has been found in the literature that a prototype molecule, N,N-dimethylnitramino, 12 self assembles through NO$_2$-N(CH$_3$)$_2$ recognition (Figure 3).$^{17}$ Interestingly the structure of this compound has also been determined by neutron and gaseous state electron diffraction techniques, besides the X-Ray diffraction method.$^{17,18}$ This abundance of structural data provided a unique opportunity to ascertain the significance of cooperative effects experimentally, that is by comparing molecular geometries of solid and gaseous state structures. In addition, the simple molecular geometry of 12 makes it easy to approximate the energetics and cooperativity of C-H...O interactions theoretically using AM1 calculations.$^{19,20}$

For a supermolecule to be formed, the molecules must initially form a dimer, then a trimer and continue to aggregate till a supramolecular struc-

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$^1$Complex 11: Monoclinic, a=11.36(2), b=10.93(2), c=11.14(1)Å; $\beta=92.32(5)^\circ$. 
Figure 3. C-H...O Hydrogen bonds (dimer X) formed in the crystal structure of N,N-dimethylnitramine. $\text{12N} = \bullet \text{ O} = \bigcirc$
re is attained. In order for this process to occur, cooperativity should play an important role in the addition of individual units to the growing aggregate. The cooperative effects in C-H...O hydrogen bond formation are discussed by considering molecular and supramolecular structures of 12 as a model (Figure 3). The H atoms of 12 point exactly towards the O atoms of the NO$_2$ group. As these H atoms are obtained from a neutron study (σ=0.036) there is little ambiguity regarding their position. The NO$_2$ and NO groups of 7 are accurately coplanar. At this stage, it may be interesting to recall the rhetorical argument of Cotton and Luck on the determination of H atom position by X-Ray and neutron diffraction methods that 'the neutron experiments sees with considerable accuracy (ca. ±0.001Å), the position of the hydrogen atoms's nucleus, the proton. In a very favorable case [...], the X-ray experiment sees with less accuracy (ca. ±0.02Å), the hydrogen atom's electron cloud. Which of these is 'the hydrogen atom'? Both the nucleus and the electron density of an atom are the essential parts and it is therefore impossible to assert rationally that the position of either one or the other is 'the' position of the atom.'

![Scheme II](image)

**Scheme II**

Charge transfer through C-H...O hydrogen bonds in the linear chain of molecules 12 in the solid state (Figure 3), causes systematic changes in supramolecular geometry of 12 compared to that of the isolated gaseous state structure (Scheme II). The intramolecular bond lengths and angles
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Observed for 12 in the solid state are in consonance with charge transfer (Table 1). The solid state structure of 12 reveals a slight decrease in N-N and N-C bonds lengths and an increase in N-O bond length compared to the gaseous state structure. In addition, the O-N-O and C-N-C bond angles of 12 in the solid state are decreased with respect to the value in the isolated molecular structure and such a decrease in bond angles may facilitate the direction of the H atoms towards the lone pairs of the O atoms, accentuating cooperativity. However, there is no elongation in the C-H bond length as might have been expected. Indeed, it is difficult to detect the cooperative effects of C-H...O bonds in the solid state unless we have an isolated molecular structure for comparison as the changes involved in bond lengths and angles are marginal. The energy gained through cooperativity in C-H...O hydrogen bonds is still quite low compared to that in strong hydrogen bonds.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Neutron</th>
<th>X-ray</th>
<th>Electron (gas)</th>
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<tbody>
<tr>
<td>N-N</td>
<td>1.326(3)</td>
<td>1.324(4)</td>
<td>1.382(3)</td>
</tr>
<tr>
<td>N-C</td>
<td>1.452(4)</td>
<td>1.457(4)</td>
<td>1.460(3)</td>
</tr>
<tr>
<td>O-N</td>
<td>1.233(5)</td>
<td>1.244(4)</td>
<td></td>
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<tr>
<td>O-N-O</td>
<td>123.7(3)</td>
<td>123.4(3)</td>
<td>130.4(6)</td>
</tr>
<tr>
<td>C-N-C</td>
<td>124.5(2)</td>
<td>124.5(3)</td>
<td>127.6(6)</td>
</tr>
<tr>
<td>C-H</td>
<td>1.081(7)</td>
<td>0.99(2)</td>
<td>1.121(5)</td>
</tr>
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</table>

The energies of O-H...O and C-H...O hydrogen bonds in complex 1 were evaluated computationally with the semi-empirical AM1 approximation.
This method has previously been used to compute energy in O-H...O hydrogen bonds of carboxylic and 1,3-diketone aggregates.\textsuperscript{10,14} It has also been shown to reproduce C-H...O interaction energies and geometries well.\textsuperscript{20} The hydrogen bond energy for the O-H...O dimer of complex 1 was found to be -6.7 Kcal/mole and that of the C-H...O dimer -2.45 Kcal/mole. It should be noted that while the O-H...O geometry and energy are poorly calculated in SCF methods because of overestimation of the H...H repulsions in the carboxy dimer ring and the neglect of electron correlation effects,\textsuperscript{136,22} there are no similar sources of error in the calculation of C-H...O bond energies. The hydrogen bonds in the optimised structure of 1 are as follows: O-H...O dimer O...O 3.04, 3.10 Å, H...O 2.07, 2.12 Å-O-H...O 174.6°, 175.0°; C-H...O dimer C...O 3.49, 3.45 Å, H...O 2.42, 2.33 Å, C-H...O 157.0, 174.7°. It is difficult to compute the cooperative effects of C-H...O bonds in complexes 1 and 2, because the size of the linear molecular aggregates impede calculations before the cooperativity limit can be reached.

The optimised C-H...O hydrogen bond energies and averaged partial charges of the O and H atoms of dimer X in the linear molecular aggregates of 12 are given in Table 2. The stabilisation per dimer unit via C-H...O hydrogen bonding increases with an increase in the number of molecules in the linear chain. A linear molecular assembly is preferred because of the additional cooperativity energy and this extra energy may discriminate against other possible molecular arrangements which do not have this cooperative advantage. The enhancement of charges on the H and O atoms from monomer to n-mers indicates mutual induction and charge transfer through C-H...O hydrogen bonds. Table 2 shows that the cooperativity effect begins to level off at the pentamer stage.
Table 2

<table>
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<tr>
<th></th>
<th>Total Energy</th>
<th>Total C-H...O Bonds Energy</th>
<th>Average C-H...O Bonds Energy (per dimer unit)</th>
<th>Atom charges</th>
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<td></td>
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<td>H</td>
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<td>monomer</td>
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<td>dimer</td>
<td>40.2</td>
<td>3.2</td>
<td>3.2</td>
<td>0.1320</td>
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<tr>
<td>trimer</td>
<td>58.0</td>
<td>7.1</td>
<td>3.6</td>
<td>0.1365</td>
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<tr>
<td>tetramer</td>
<td>75.4</td>
<td>11.4</td>
<td>3.8</td>
<td>0.1384</td>
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<tr>
<td>pentamer</td>
<td>93.1</td>
<td>15.4</td>
<td>3.9</td>
<td>0.1395</td>
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2.2.2 C-H...O Hydrogen Bond Patterns in Complexes 4-9

The NO2 group in complexes 4-9 is particularly suited for the formation of C-H...O hydrogen bonds and in general, three distinct patterns of C-H...O bonds have been observed. The choice between these three C-H...O patterns seems to depend on the stoichiometry and arrangement of the functional groups (mostly -NO2) in the respective complexes 4-9. Complex 10 formed twinned crystals and only an approximate structural analysis was possible and for this reason its C-H...O interaction patterns are not discussed here.\(^2\)

The first pattern (Figure 4a) is found in complexes of 3,5-dinitro-substituted benzoic or cinnamic acids with 4-N(CH3)2-substituted benzoic or cinnamic acids (4, 5, 9) and is characteristic of the NO2 to N(CH3)2 approach. The C-H...O bonds in this first pattern involve mainly sp\(^3\) H atoms of the -N(CH3)2 groups and -NO2 O atoms (Complex 5; C...O; 3.68, 3.50, 3.79, 3.60, 3.37Å: C-H...O; 157, 161, 132, 166, 132°).

The second pattern is a self-motif found in all complexes containing 3,5-dinitrocinamnic acid 2b (4, 5 and 6, Figure 4b). This pattern is charact-

\(^2\)Complex 10: Monoclinic, P2\(_1\)/c, \(a= 7.89(1), b= 16.55(2), c= 14.41(1)\)Å; \(\beta= 97.31(1)\)°.
Figure 4 Three types of C-H...O bonding patterns observed in complexes 3-9.
(a) Recognition pattern of 3,5-dinitro to 4-NMe₂ in complexes 4, 5 and 9. (b) Self assembly of 2b molecules in 4, 5, 6 and in acid 2b. (c) Self assembly of 2b molecules with two types of motifs in 7 and 8. N = ◦ O = ⊗
erised by translation of 8.3 to 8.4 Å and involves linear C-H...O bonds between both O atoms of a particular NO₂ group with the styryl and aromatic H atoms of the translated neighbour (Complex 4; C...O; 3.50, 3.50 Å: C-H...O; 173, 167°). This pattern is also found in the crystal structure of the free acid 2b⁷ and can be considered to be a molecular ribbon obtained by self-assembly.

That the arrangement of NO₂ groups in a molecule is also critical in determining the C-H...O pattern, is clear on inspection of Figure 4c which illustrates the third C-H...O pattern in these complexes, a pattern characteristic of the isomeric 2,4-dinitrocinnamic acid 2c (7 and 8, Complex 7; C...O; 3.52 Å: C-H...O; 162°). The 2,4-arrangement of NO₂ groups results in a different C-H...O pattern than is obtained for the 3,5-arrangement shown in Figure 4b. In fact, there are two motifs, but both involve inversion-related molecules. One of the motifs involves an O atom of the 4-NO₂ group and the H3 atom while the other involves the carboxyl O and H6 and H8.

These three patterns along with NO₂-N(CH₃)₂ pattern are exclusive to each of the four substitutional categories described above and it is noteworthy that the particular pattern obtained depends not only on the stoichiometry (one or two NO₂ groups) but also on the arrangement of groups (2,4-dinitro or 3,5-dinitro). C-H...O networks in complexes 4-9 are therefore predictable and consequently C-H...O bonds can be well-utilised for molecular recognition and self-assembly in related organic solids. The non-centrosymmetric nature of some of these C-H...O patterns (Figures 1, 4a and 4b) may also be exploited for the deliberate design of non-centrosymmetric crystals leading to NLO materials.¹⁶ These recognition patterns also highlight an interesting common feature and that is, the more acidic protons on the nitro-substituted acids, (especially acids 2b and 2c) are actively involved in the molecular recognition process and support arguments that hydrogen atom acidity is more important than O-atom basicity in the formation of
C-H...O bonds.\textsuperscript{46,23}

### 2.2.3 A General Study of C-H...O Recognition Patterns

It has been observed that the C-H...O hydrogen bonds in NO\textsubscript{2} groups frequently show patterns I-V.\textsuperscript{6,243} Thus, an exhaustive search was carried out with the CSD on recognition patterns that are characteristic of functional groups (pattern I) and geometry (patterns II-V). The recognition features of these patterns are now described.

\[ \text{Starred atoms can be either (a) } \text{sp}^3 \text{ or (b) } \text{sp}^3 \text{ hybridised.} \]
2.2.3.1 Binding Features of Pattern I

The CSD was searched to find out the occurrence and the geometrical specificity of pattern I in NO$_2$ and N(CH$_3$)$_2$ compounds. Of the 69 unique structures considered (see Section 2.4.5), motif I is found in 29 compounds whose bibliographic information is given in Table 3. The NO$_2$- N(CH$_3$)$_2$ approach can be described in terms of three parameters: (1) The interplanar angle between the NO$_2$ and NC$_2$ planes with H atoms ignored. Figure 5a represents a histogram of the interplanar angles; (2) The vertical offset or the translation perpendicular to the NO$_2$/NC$_2$ plane. To represent this offset we have calculated the average interplanar distances of the NO$_2$ and NC$_2$ planes. These distances are shown in histogram 5b; (3) The lateral offset of NO$_2$ and NC$_2$ groups that is, the translation in the mean NO$_2$/NC$_2$ plane. This parameter may be described in terms of the difference between the distances of diagonally disposed C and O atoms of pattern I, C1...O6 and C3...O5. This is shown in Figure 5c. Small differences in these diagonal distances indicate more symmetrical C-H...O dimers with little lateral offset between NO$_2$ and NC$_2$ groups while large differences in diagonal distances indicate more unsymmetrical C-H...O dimers.

It is clear from Figure 5a that the NO$_2$ and NC$_2$ groups prefer to be in plane (most of the points lie below 15°). Figure 5b indicates that there is hardly any vertical offset between NO$_2$ and NC$_2$ groups as most of the points cluster within 0.20Å of a coplanar arrangement. In contrast, lateral offsets are common and Figure 5c shows that many points are scattered with lateral offsets between 0.10 and 1.80 Å. The lateral offset arrangement in pattern I is possibly stabilised by additional bifurcated C-H...O interactions as in complex 2. A superposition stereoplot of pattern I viewed along the plane of the NO$_2$ group for all the 29 compounds with the NO$_2$ group being fixed, is shown in Figure 6. This plot facilitates a visualisation of the relative orientation of the NO$_2$ and NC$_2$ groups.
Figure 5 Histograms of three parameters which represent the NO$_2$-NC$_2$ approach in pattern I. (a) Interplanar angle (°) between NO$_2$ and NC$_2$ planes. (b) Vertical offset translation (Å) perpendicular to NO$_2$/NC$_2$ planes. (c) Lateral offset translation (Å) in the NO$_2$/NC$_2$ planes.
Figure 6. Stereodiagram of a superposition plot of NO$_2$ and NC$_2$ fragments of pattern I in 29 compounds. The plane of the NO$_2$ group is perpendicular to the plane of the paper and this NO$_2$ plane is kept fixed from structure to structure. 

N = ○ O = ⊙
<table>
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<th>Bibiligraphic Information on Nitro compounds containing Pattern I</th>
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<tbody>
<tr>
<td><strong>CADFOC</strong>: 1, 1, 5, 5-Tetramethyl-1, 2, 5-triazapentadienium picrate; C6 H14 N3 1+, C6 H2 N3 O7 1-; R.O.Gould, H.McNab, M.D.Walkinshaw; Acta Cryst., C (Cr.Str.Comm.), 39, 1097, 1983.</td>
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<tr>
<td><strong>DADZIR</strong>: E, E-1-(p-Dimethylaminophenyl)-5-(o-hydroxyphenyl)-penta-l, 4-dien-3-one m-dinitrobenzene clathrate; C19 H19 N1 O2, C6 H4 N2 O4; F.H.Herbstein, M.Kapon, G.M.Reisner, M.B.Rubin; J.Inclusion Phenomena, 1, 233, 1984.</td>
</tr>
<tr>
<td><strong>DUPHIF</strong>: 1, 1-bis(Dimethylamino)-2-nitroethylene; C6 H13 N3 O2; F. Ganazzoli, S. V.Meille, P.Gronchi ; Acta Cryst., C (Cr.Str.Comm.), 42, 1385, 1986.</td>
</tr>
<tr>
<td><strong>FAJYIY</strong>: N, N-Dimethyl-4-(1-(p-nitrophenyl)ethylene)aniline; C16 H16 N2 O2; Yun Yi Wei, B.Tinant, J.P.Declercq, M.Van Meerssche; Acta Cryst., C (Cr.Str.Comm.), 43, 86, 1987.</td>
</tr>
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</table>
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FAWWIJ: N, N-Dimethyl-2, 4-dinitro-3-toluidine; C9 H11 N3 O4; J.K. Maurin, T.M. Krygowski; Acta Cryst., C (Cr.Str.Comm.), 43, 64, 1987.


JISZAM: rac-1H-1-Hydroxy-2, 3-dihydro-2, 2, 3-trimethyl-7-methoxyisoidolium 3, 5-dinitrobenzoate; C12 H18 N1 O2 1+, C7 H3 N2 O6 1-; J.D. Carroll II, P.R. Jones, R.G. Ball; J. Org. Chem., 56, 4208, 1991.

JOLNED: 3, 3-Dimethyl-1-(4-nitrophenyl)triazene; C8 H10 N4 O2; S. Neidle, D.E.V. Wilman; Acta Cryst., B (Str. Sci.), 48, 213, 1992.


MACINA10: 4- Dimethylamino-3-nitrocinnamic acid; C11 H12 N2 O4; C.P. Huber; Acta Cryst., C (Cr.Str.Comm.), 41, 1076, 1985.

MANCPP: Methyl-(2E, 4Z)-5-dimethylamino-2-nitro-4-(4-chloro-2-nitrophenyl)-2, 4-pentadienoate; C14 H14 Cl1 N3 O6; U. Hengartner, A.D.


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### 2.2.3.2 Binding Features of Patterns II-V

The present analysis is statistical in nature and enables us to formulate the most frequent recognition patterns of NO₂ groups, which may be useful in crystal engineering. Patterns II-V are divided according to C-H group hybridisation, i.e. sp² and sp³ to visualise the impact of H atom acidity in C-H...O bond formation. Table 4 presents some pertinent details.

Figure 7 shows that the patterns IIa and IIb are largely characterised by symmetrical C-H...O interactions, that is those with d₁ = d₂ and θ₁ = θ₂ (see Experimental Section for a definition of these terms). This plot indicates that pattern II is preferably centrosymmetric. The number of hits obtained
Figure 7. Scatterplots of C...O distances of pattern II; $d_1 = C6...O2(\text{Å})$, $d_2 = C5...O9(\text{Å})$. (a) Motif IIa with sp$^2$ C-H. (b) Motif IIb with sp$^3$ C-H. The linear relationship of $d_1$ and $d_2$ indicates the significance of centrosymmetric contacts for this motif. Notice that there are far fewer points in IIb than in IIa.
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Table 4

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<th>Statutory Data on Patterns I-V in Nitro Compounds</th>
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|                  | Number of compounds with a potential to form pattern | Number of compounds which actually display pattern | Average hydrogen bonded parameters
|                  |                                              |                                              | C...O (Å) | C-H...O (°) |
| I                | 69                                             | 29                                             | 3.65      | 138.0      |
| IIa              | 817                                            | 280                                            | 3.52      | 127.5      |
| IIb              | 88                                             | 25                                             | 3.61      | 125.8      |
| IIIa             | 177                                            | 50                                             | 3.45      | 128.0      |
| IIIb             | 33                                             | 0                                              | -         | -          |
| IVa              | 136                                            | 19                                             | 3.59      | 137.6      |
| IVb              | 103                                            | 10                                             | 3.66      | 135.9      |
| Va               | 136                                            | 68                                             | 3.50      | 135.1      |
| Vb               | 103                                            | 0                                              | -         | -          |

@ contact is considered a C-H...O hydrogen bond if 3.0 ≤ C...O ≤ 4.0Å and 100 ≤ C-H...O ≤ 180°.

for IIb are reduced significantly compared to IIa because in that case the C-H group is specified to be sp³ hybridised. Interestingly most of the hits observed for IIb correspond to cyclopropane derivatives (where strictly speaking the C-H group closely resembles alkenes rather than alkanes) and rigid alicyclic compounds like cubanes and prismanes.

Pattern III is similar to II except that one of the NO₂ groups is replaced by a C=O group to give a non-centrosymmetric motif. The number of hits obtained for IIIa suggest that this is also a potential building block for molecular recognition and most of the hits observed in this case correspond to esters of nitroaromatic compounds. It may be mentioned here that we have succesfully employed such C-H...O hydrogen bonds in the solid state supramolecular assembly of molecular complexes of 1,3,5-trinitrobenzene and dibenzylideneacetone (Scheme III)."
There is a very close relationship between patterns IV and V as both motifs involve similar molecular fragments. Two O atoms of the NO₂ group interact with two H atoms in IV, while only one O atom of the NO₂ group interact with two H atoms in V (this may be termed an acceptor-bifurcated interaction according to the nomenclature of Saenger and Jeffrey).\(^8\) The number of hits obtained for these motifs suggest that pattern V is preferred to IV. It should be recalled that pattern I which is geometrically similar to motif IV also prefers to form bifurcated interactions (Figures 2 and 5). It seems then that the disposition of H atoms in patterns I and IV or V is conducive to acceptor bifurcation and this is in contrast with the general observation that the H atom (either C-H or O-H) prefers to interact with two O atoms (proton bifurcation).\(^15\) This possibility for bifurcation does not exist for dimer motifs II and III.

Scheme III
2.2.4 Nitro Group Crystal Engineering

We now discuss a few occurrences of pattern I to highlight different aspects of this motif. The NO₂ and N(CH₃)₂ groups in 13 are sterically crowded, the molecular structure is non-planar and hence the I modules in the crystal are three dimensionally disposed (C...O, C-H...O; 3.73, 3.66Å, 123.9, 173.6° and 3.68, 3.81Å, 143.6, 142.3°). This is shown in Figure 8. The aromatic rings of 14 are mutually perpendicular and the molecule has a bent conformation. The crystal structure of 14 (Figure 9) has a sinusoidal chain with NO₂ and NC₂ planes being out of plane with an angle of 70.5° between them (C...O, C-H...O: 3.60Å, 3.72 Åand 147°, 141°). The planar molecule 15 forms an acentric linear chain with NO₂ and NC₂ groups being in-plane. Interestingly, when the N(CH₃)₂ group of 15 is replaced by a CH₃ group, (i.e, molecule 16) motif V is adopted. These examples hint that pattern I can be used to steer the crystal packing reliably if the organic molecules bear only NO₂ and N(CH₃)₂ functional groups.

We will now try to address the role of C-H...O hydrogen bonding patterns in nitro group crystal engineering. For this purpose, the crystal structures of compounds 17-20 were chosen. These examples delineate various aspects of patterns II-V and are potential feedbacks in the deliberate design of nitro
Figure 8. Stereoview of the crystal structure of alkene 13 to show pattern I.

Notice the two dimensional molecular arrangement.
Figure 9. Stereoview of the crystal structure of thioether 14 to show the sinusoidal chain of molecules linked by pattern I. Note that the NO\textsubscript{2} and NC\textsubscript{2} planes are perpendicular to each other.
containing C-H...O mediated supermolecules. Molecule 17 manifests all three patterns IIa, IIb and Va in its crystal structure (Figure 10). The molecular and supramolecular structures of 18 are very interesting in that two types of intramolecular phenyl-phenyl interactions are present. The two unsubstituted phenyl rings are involved in herringbone interactions and the nitrophenyl rings are involved in stacking interactions. Curiously, these two stacked nitrophenyl moieties self assemble using motif IIIa as shown in Figure 11 (one of the O atoms is ethereal). Additionally, the crystal structure also displays pattern IIa (not shown in Figure 11 for the sake of clarity). The crystal structure of 19 shows a linear chain that has mutually perpendicular O-H...O and C-H...O dimers (IIb) in the chain (Figure 12). The reason for this is that both the NO₂ and CO₂H groups are substituted on a single C atom of the cyclopropane ring and have a strong preference for linear and planar O-H...O and C-H...O dimer formation. The dimer of molecule 20 is shown in Figure 13 and exhibits patterns IV and/or V with good C-H...O interactions in addition to intramolecular N-H...O interactions. This example indicates that if the strong proton donors are constrained by intramolecular factors, it is possible that C-H...O recognition patterns of the NO₂ group will determine the molecular assembly and in the present case
Figure 10. Stereoview of the crystal structures of 17. Note that the molecules are stabilised by all three patterns IIa, IIb and V.
Figure 11. Stereoview of the crystal structure of diester 18. Notice the appearance of pattern IIIa.
Figure 12. Stereoview in the crystal structure of cyclopropane 19 to show the linear chain arrangement. The chain is linked by carboxyl dimers and IIb dimers. These two dimers are mutually perpendicular.
Figure 13. A dimer of 20 formed by C-H...O interactions in the crystal. This dimer reveals motifs IV and/or V which possibly stabilise the planar arrangement. The N-H...O bonds are intramolecular. $N = \bullet O = \text{H}$
Molecular Recognition in Crystalline Nitro Compounds

it may be reasonable to assume that the planar dimer of 15 is a result of good lateral C-H...O interactions of the NO\textsubscript{2} group with intermolecular N-H...O interactions playing a passive role.

The statistical analysis given in Table 4 on the C-H...O hydrogen bonded motifs I-V clearly indicates that the H atom acidity and a rigid molecular geometry are crucial for the establishment of C-H...O recognition patterns. As Table 4 suggests, there are a small number of hits or no hits at all for fragments with sp\textsuperscript{3} hybridised C-H groups. However, the electron-withdrawing nature of the NO\textsubscript{2} group enhances the H atom acidity and may promote the possibility of selective binding in this class of compounds. The larger number of hits obtained for I and II\textsubscript{b}, despite their low acidity C-H groups indicates the importance of a rigid molecular framework. Many of the hits obtained in this study correspond to simple nitro-substituted compounds, with only sp\textsuperscript{2} C atoms and it is suggested that such molecules which have the possibility of forming only C-H...O interactions (and no other directional interaction) can be used to design supermolecules with high precision (Scheme III). However, C-H...O recognition patterns can also be designed with success in the presence of strong interactions if these strong interactions do not interfere with either H or O atoms of patterns I-V. For example, complexes 1, 2 and 19 (Figures 1, 2 and 12) form carboxyl dimers but the C-H...O recognition patterns are intact. Similarly in ester 18, the major non-bonded interactions (van der Waals and π...π) are optimised in the molecular conformation itself and their role in crystal packing is reduced with the result that the weakly directional C-H...O interactions can form pattern III\textsubscript{a} (Figure 11). While the crystal structure of 20 has intramolecular N-H...O hydrogen bonds, their role in crystal packing is undermined; consequently, C-H...O interactions play a key role in dimer formation (Figure 13). These examples suggest that one has to keep track of all the possible interactions of a molecule for efficient solid state supramolecular design. It is also to be mentioned here
that if the recognition patterns I-V are assisted by additional C-H...O hydrogen bonds, that is by a matching of multiple C-H...O interactions in a single recognition pattern, supramolecular design would be very efficient as shown in scheme III.

2.3 Conclusions

The present study unequivocally demonstrates that weak C-H...O bonds are potential interactions for molecular recognition studies. C-H acidity is important in C-H...O recognition patterns which are additionally sensitive to the C:H:O stoichiometry and substitution pattern of functional groups in the molecular skeleton. These interactions can be efficiently used in the absence of strong intermolecular interactions or if strong interactions do not interfere with the C-H...O recognition patterns. Though the patterns suggested in this study involve only NO$_2$ O atoms, the idea can be extended to explore many new C-H...O building blocks with other types of O atoms. The general observations made on C-H...O recognition patterns in this analysis may facilitate the design of new materials based on these interactions and help in understanding and predicting secondary and tertiary structural features of many organic and bio-organic supermolecules with more reliability.

It is concluded then that weak C-H...O bonds too exhibit cooperativity and charge-transfer like strong hydrogen bonds and that better computational estimates of these interactions can be obtained only by considering multi-molecular aggregates.
2.4 Experimental Section

2.4.1 Synthesis of Acid Monomers

These were either purchased (1a - 1c) or prepared (2a - 2f) from the corresponding aldehydes by Knoevenagel condensation.29

Preparation of 3,5-dinitrobenzaldehyde:

A solution of 3,5-dinitrobenzoic acid (30 mmol, 6.36g) dissolved in dry THF (100 mL) was taken in a two-necked round-bottomed flask equipped with a condenser, diborane gas inlet and a side arm for passing N2. Diborane gas was generated by dropwise addition of I2 (30 mmol, 7.62g) in diglyme (100 mL) to NaBH4 (60 mmol, 2.28g) in diglyme (30 mL). This diborane gas was bubbled into the acid solution for 3-5 h at 0°C. The reaction mixture was stirred for 5 h even after the bubbling of diborane gas ceased. The reaction mixture was carefully quenched with water (2 mL) and 3N HCl (5 mL) and the organic layer was extracted with ether. The combined organic extract was dried over anhydrous MgSO4 and evaporation of ether solvent resulted in the pale-yellow coloured 3,5-dinitrobenzyl alcohol which was recrystallised from a 1:1 mixture of hexane-ether (m.p. 81°C). NMR (CDCl3): δ 4.97 (s, 2H), 8.3 (m, 2H), 9.0 (m, 1H).

In a 100 mL round-bottomed flask fitted with a reflux condenser was suspended 6.46g (30 mmol) of PCC in 40 mL of anhydrous CH2Cl2. 3,5-dinitrobenzyl alcohol (20 mmol, 3.96g) was added in one portion to the stirred solution. After one hour, 40 mL of dry ether were added and the supernatant liquid decanted from the residual blackgum. The insoluble residue was washed thoroughly three times with 10 mL portions of anhydrous ether. The combined organic solution was passed through fluorosil and the solvent removed by distillation. The 3,5-dinitrobenzaldehyde obtained was recrystallised from 1:2 toluene-hexane (m.p. 81°C). NMR (CDCl3): δ 9.05 (m, 1H), 9.29 (m, 2H), 10.21 (s, 1H).
Pyridinium Chlorochromate (PCC): To 184 mL of 6N HCl (1.1 mol) was added 100 g (1 mol) of CrO₃ rapidly with stirring. After 5 minutes the homogeneous solution was cooled to 0°C and 79.1 g (1 mol) of pyridine was carefully added over 10 minutes. Re-cooling to 0°C gave a yellow-orange solid which was collected on a sintered glass funnel and dried for one hour in vacuum.

2.4.2 Preparation of 1:1 Acid Complexes

Complex 1: Orange-yellow crystals of complex 1 (m.p. 235°C) were obtained readily from an equimolar solution of acids 1a and 1c in MeOH.

Complex 2: Violet crystals of complex 2 (m.p. 181-183°C) were obtained from an equimolar solution of acids 1a, and 2d in toluene-MeOH.

Complex 3: Violet crystals of complex 3 (m.p. 245°C) were obtained from an equimolar solution of acids 2a, and 2d in MeOH, but these were too thin for X-Ray work.

Complex 4: Violet crystals of complex 4 (m.p. 200-202°C) were obtained from an equimolar solution of acids 2b and 1c in MeOH.

Complex 5: Violet crystals of complex 5 (m.p. 175-177°C) were obtained from an equimolar solution of acids 2b and 2d in EtOH.

Complex 6: Deep-yellow crystals of complex 6 (m.p. 159°C) were obtained from an equimolar solution of acids 2b and 2e in 2:3 toluene-benzene.

Complex 8: Deep-yellow mixed crystals of complex 8 (m.p. 143°C) were obtained from an equimolar solution of acids 2c and 2e in EtOH.

Complex 9: Violet mixed crystals of complex 9 (m.p. 201-202°C) were obtained from an equimolar solution of 1b and 1c in MeOH.

Complex 10: Violet mixed crystals of complex 10 (m.p. 145°C) were obtained from an equimolar solution of acids 1b and 2d in toluene. These crystals were found to be twinned.

Complex 11: Black-violet crystals of complex 11 (m.p. 148°C) were ob-
tained from an equimolar solution of 1,4-dinitrobenzene and N,N,N',N'–
tetramethyl-p-phenylenediamine in CCl$_4$-hexane. These crystals were found
to be twinned.

All the above complexes can also be prepared by thorough grinding of
their respective components. The X-Ray powder spectra of both the single
crystalline and ground materials are identical. The complexation is very
vigorous in the case of complex 11 where even mild rubbing of the starting
materials leads to a quantitative solid state reaction.

2.4.3 X-Ray Crystallographic Studies on Acid Complexes

The data for the complexes, 1, 2, 4, 8 and 9 were collected by Dr. T.
Pilati, University of Milano, Italy while the data for complexes 5 and 6 were
collected by, Dr. D.E. Zacharias, Fox Chase Cancer Centre, Philadelphia,
U.S.A. and Dr. W.T. Robinson, University of Canterbury, Christchurch, New
Zealand respectively. Complex 7 has already been reported from this lab-
oratory. The structure solution of all the complexes was carried out in
this study with SHELXS86 and the refinements were carried out with
SHELX76. All non-hydrogen atoms were refined anisotropically and the
final R-factors and other crystallographic information is presented in Ap-
pendix A-1. Tables of coordinates and thermal vibrational parameters are
given Appendix A-2.

2.4.4 Semi-empirical Calculations

The AM1 approximation to molecular orbital theory was used in this
study to evaluate the energies of the O-H...O and C-H...O hydrogen bonds
in complex 1. All the calculations were carried out using the MOPAC
program. The geometry of the O-H...O and C-H...O dimers in the crystal
structure of complex 1 was the starting point in the optimisation. The C-
H...O bond energy of the dimer was evaluated by subtracting the energies of
the individual monomers. Cooperative effects in C-H...O bonds were evaluated by considering linear aggregates of 12. Such aggregates are segments of the actual crystal structure which consists of a linear array of molecules (Figure 3). The neutron structural data of 12 were taken as input for the optimisation of linear C-H...O bonded molecular aggregates and up to five monomer units were considered to determine the magnitude of the cooperative effects.

2.4.5 CSD Studies

Screens -28, 153, 85 and 88 were set to eliminate organometallic entries and structures without coordinates or unmatched chemical and crystallographic connectivities. Entries with R-factors greater than 0.10 were also excluded to create a subsidiary IDX file of 2306 nitro compounds. All further 3D graphical searches for NO2 recognition patterns I-V were made from this subsidiary file. For determining *bona fide* C-H...O interactions, C...O distances 3.0 ≤ 4.0 Å and C-H...O angles of 100 ≤ 180° were considered. The motifs I-V are characterised by two C...O distances $d_1$ and $d_2$ and two C-H...O angles $\theta_1$ and $\theta_2$. For example, motif II can be defined by $d_1 = C_6...O_2$, $d_2 = C_5...O_9$ and $\theta_1 = C_6-H_12-O_2$ and $\theta_2 = C_5-H_11-O_9$. Using such criteria, patterns such as IV and V may be distinguished.

There are 84 entries that contain both NO2 and N(CH3)2 functional groups and of these, fifteen are duplicates and were not considered any further. For example, the structure of 12 has been determined as many as eight times by neutron and X-Ray methods but we have considered only the best structure here. The coordination of H atoms was specified to be either T3 or T4 to get $sp^2$ or $sp^3$ hybridised C atoms for these four patterns. Suffixes a and b are used in motifs II-V to distinguish $sp^2$ and $sp^3$ C-H groups.
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30. It has been shown that mechanical grinding is a superior method of obtaining quantitative yields of many organic donor-acceptor complexes. Naturally only polycrystalline material is obtained.

